



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

OCT 3 2003

Food and Drug Administration  
College Park, MD 20740

Jonathan W. Emord, Esq.  
Emord & Associates, P.C.  
5282 Lyngate Court  
Burke, VA 22015

Date:

Re: Health Claim Petition: Glucosamine and Chondroitin Sulfate, and (1)  
Osteoarthritis; (2) Osteoarthritis-related joint pain, tenderness, and swelling; (3)  
joint degeneration; and (4) cartilage deterioration

Dear Mr. Emord:

This letter responds to the health claim petition you submitted on behalf of Weider Nutrition International, Inc. (the petitioner) pursuant to section 403(r)(5)(D) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 343(r)(5)(D)) with respect to claims concerning the relationships between the consumption of glucosamine and chondroitin sulfate and reduction in the risk of: osteoarthritis; osteoarthritis-related joint pain, joint tenderness, and joint swelling; joint degeneration; and cartilage deterioration. The Food and Drug Administration (FDA) received your petition on May 29, 2003.

As provided for in section 403(r)(4)(A)(i) of the Act and 21 CFR 101.70(j)(2) of FDA's regulations, FDA will notify the petitioner within 100 days of the receipt of a health claim petition that the petition has either been filed for comprehensive review or denied. If FDA does not act within 100 days, the petition is deemed to be denied unless an extension is mutually agreed upon by FDA and the petitioner. We have calculated the 100-day date for your petition to be September 6, 2003. By mutual agreement, the date for FDA's decision on filing this petition has been extended until October 3, 2003.

In accordance with 21 CFR 101.70(j)(2), we are denying your petition. Based on the subject matter of your proposed claims and the nature of the scientific evidence you present to support them, we conclude that your proposed claims are drug claims rather than health claims. As you know, in 2000, FDA issued a health claim petition denial concluding that claims about treatment or mitigation of an existing disease do not fall within the scope of the health claim provisions in section 403(r) of the Act (21

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USC 343(r)) but rather must be regulated as drug claims.<sup>1</sup> The agency's position was upheld by the district court in ensuing litigation, and the case is now pending on appeal. See Whitaker v. Thompson, 239 F. Supp. 2d 43 (D.D.C. 2003), *appeal docketed*, No. 03-5020 (D.C. Cir. Jan. 14, 2003). We have attached copies of the denial letter and of FDA's brief on appeal, with which you are familiar. These explain the reasons for FDA's conclusion that claims about effects on existing diseases must be regulated as drug claims and not health claims.

Based on our review of your petition, including both the subject matter of your proposed claims and the nature of the scientific evidence you present to support them, we conclude that your claims are outside the scope of the health claim provisions in section 403(r) of the Act because these claims concern treatment or mitigation of an existing disease, osteoarthritis, rather than reducing the risk of contracting that disease. In accordance with section 201(g)(1)(B) of the Act (21 USC 321(g)(1)(B)), which defines "drug" in part as an article intended for use in the treatment or mitigation of disease, claims that suggest that glucosamine and chondroitin sulfate are useful in treating or mitigating osteoarthritis subject products bearing such claims to regulation as drugs.

## **I. Background**

### **A. Definition of Osteoarthritis**

Osteoarthritis (OA) is a complex disease, which the National Institutes of Health (NIH) defines by its symptoms or pathology.<sup>2</sup>

"The pathology of osteoarthritis involves the whole joint in a disease process that includes focal and progressive hyaline articular cartilage loss with concomitant changes in the bone underneath the cartilage, including development of marginal outgrowths, osteophytes, and increased thickness of the bony envelope (bony sclerosis). Soft-tissue structures in and around the joint are also affected. These structures include synovium, which may show modest inflammatory infiltrates; ligaments, which are often lax; and bridging muscle, which becomes weak. Many people with pathologic and radiographic evidence of osteoarthritis have no symptoms. From a clinical perspective, the most compelling definition of disease is one that combines the pathology of disease with pain that occurs with joint use. Unfortunately, the cause of pain in osteoarthritis is unknown." (Felson *et al.*, 2000)

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<sup>1</sup>See letter from Joseph Levitt, Director, FDA Center for Food Safety and Applied Nutrition, to Jonathan Emord, Emord & Associates (May 26, 2000) (copy attached).

<sup>2</sup>Felson DT, Lawrence RC, Dieppe PA, et al. Osteoarthritis: New Insights. Part 1: The Disease and Its Risk Factors. *Ann Internal Med* 2000;133(8):635-646.

## **B. Etiology of Osteoarthritis**

It is unclear whether osteoarthritis is a single disease or many disorders with a similar final common pathway (Felson *et. al.*, 2000). Therefore, the precise molecular mechanisms leading to the clinical manifestations of OA are not known. However, there is a general consensus in the scientific community that osteoarthritis-related joint pain, tenderness, and swelling are not diseases themselves, but in fact, are symptoms of the disease of osteoarthritis.<sup>3</sup>

Degenerative structural changes (e.g., joint degeneration and cartilage deterioration) are responsible for OA progression and, as such, are signs of the disease of osteoarthritis that may contribute to its symptoms. However, in the absence of concurrent pain that occurs with joint use, degenerative structural changes alone are not a sufficient basis to identify the presence or absence of OA in an individual. Thus, joint degeneration and cartilage deterioration are not diseases, but rather can be considered only as important components of the symptoms of OA.

## **C. Risk Factors for Osteoarthritis**

Certain risk factors for OA have been identified, including trauma, anatomic/postural abnormalities, obesity, and genetic predisposition. Serious joint injury can lead to OA; however, OA usually results from a combination of systemic<sup>4</sup> and joint-related factors. Genetic factors have been estimated to account for about half of OA in the hands and hips and a smaller percentage of OA of the knees. Persons who are overweight have a high prevalence of OA. Biochemical markers of cartilage or bone metabolism are receiving much attention as potential risk factor biomarkers for the development of OA but, to date, there are no validated biochemical biomarkers that can be used as risk factors for development of OA (Felson *et. al.*, 2000). Thus, at this time, there are no validated and accepted surrogate disease biomarkers to credibly identify the presence or absence of OA, and consequently risk reduction in OA.

## **II. Agency Decision**

### **A. The Proposed Claims for Glucosamine and Chondroitin Sulfate Relate to Treatment or Mitigation of Disease, not Risk Reduction**

Despite the wording of your proposed claims suggesting that glucosamine and chondroitin sulfate “reduce the risk” of developing OA and related conditions, the claims

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<sup>3</sup> As FDA stated in its final rule on structure/function claims for dietary supplements, joint pain is a characteristic symptom of osteoarthritis. See 65 Fed. Reg. 1000 at 1030 (January 6, 2000).

<sup>4</sup> Examples of systemic factors include age, sex, ethnic characteristics, bone density, estrogen replacement therapy (in post-menopausal women), and genetics (Felson *et al.*, 2000).

do not, in fact, relate to reducing that risk when evaluated in light of the available science about OA. All of the conditions named in your claims (other than OA itself) refer to characteristic signs or symptoms of that disease, i.e., osteoarthritis-related joint pain, joint tenderness, and joint swelling; joint degeneration; and cartilage deterioration. None relates to any of the risk factors for OA that have been identified in the scientific literature, such as trauma, anatomic/postural abnormalities, obesity, and genetic predisposition.

The subject matter of the claims (signs and symptoms of OA) and the inclusion of the phrase “osteoarthritis-related” in the claim about joint pain, tenderness, and swelling indicate that the claims are aimed at people who already have OA and are experiencing its symptoms, not those who are at risk of developing it. Your proposed claims are clearly aimed at correcting abnormal physiological and biochemical functions--joint pain, tenderness, and swelling, joint deterioration, and cartilage deterioration--that are caused by OA or characteristic of OA. Accordingly, the claims do not, in fact, relate to risk reduction in a non-OA population.

In its 1994 final rule on health claims for dietary supplements, FDA said that claims to “correct an abnormal physiological function caused by a disease or health-related condition” would be drug claims rather than health claims. 59 FR 395 at 407-08 (January 4, 1994). With respect to claims about effects on symptoms of disease, the agency said:

[T]here is no provision in the act for the agency to exempt statements about symptoms of disease from causing products to be regulated as drugs. Although such statements may not be claims that the product will treat the disease that causes the symptoms, the statements clearly pertain to the mitigation of disease by addressing the symptoms caused by the disease. Section 201(g)(1)(B) of the act provides, in part, that articles intended for use in the mitigation of disease are drugs. (59 FR 395 at 413)

Your proposed claims about osteoarthritis-related joint pain, tenderness, and swelling; joint degeneration; and cartilage deterioration explicitly describe the mitigation of OA by treating its symptoms and thereby establish the intended use of glucosamine and chondroitin sulfate products bearing the claims as drugs.

#### **B. The Evidence Supporting the Petition Also Relates to Mitigation or Treatment of Disease and Not Risk Reduction**

FDA’s review of the scientific data in your petition confirms our conclusion that your proposed claims for glucosamine and chondroitin sulfate concern disease treatment or mitigation and not risk reduction. The clinical intervention trials cited in the petition were all conducted in individuals suffering from OA, and all relate to treatment or mitigation of OA and its symptoms. There is no evidence provided in your petition, nor

do we know of any evidence available elsewhere, relevant to whether glucosamine and chondroitin sulfate reduce the risk of developing osteoarthritis in a healthy population.

If your claims were, in fact, directed at those at risk of developing OA and related conditions, the scientific information you have submitted in your petition would be inadequate because it contains no studies or clinical data supporting a reduction in OA-related risk or risk factors. As discussed above in section I.C, at this time there are no validated and accepted surrogate biomarkers to credibly identify the presence or absence of OA, and consequently no credible measures of risk reduction for OA. Further, in order for the results from treatment or mitigation studies conducted in diseased individuals suffering from OA to be considered relevant to predicting the effectiveness of glucosamine and/or chondroitin sulfate in reducing the risk of developing OA in healthy individuals, studies would be needed to demonstrate (1) that the mechanism(s) of action(s) for the treatment and/or mitigation of OA are the same mechanism(s) of action involved in protection against development of OA; and (2) that glucosamine and chondroitin sulphate affect these mechanisms in the same way in both OA patients and in healthy people. No such studies were submitted with your petition, and FDA was not able to identify any such studies elsewhere in the scientific literature. Thus, FDA concludes that there is no credible evidence that glucosamine and chondroitin sulfate reduce the risk of developing OA in a healthy population.

### III. Conclusion

In summary, we are denying your petition because your proposed claims, like your supporting evidence, relate to mitigation or treatment of disease, not risk reduction. As such, they fall outside the health claim definition and must be regulated as drug claims.

Please feel free to contact Dr. Kathleen Ellwood, the Director of the Division of Nutrition Programs and Labeling, at 301-436-1450 if you have questions concerning this letter.

Sincerely yours,

A handwritten signature in black ink, appearing to read "L. Robert Lake". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

L. Robert Lake

Director

Office of Regulations and Policy

Center for Food Safety

and Applied Nutrition